Placenta Perfusion

Ex vivo System for Physiological Analyses of Materno-Fetal Transfer of Substances

Christian Wadsack, Uwe Lang, Department of Obstetrics and Gynecology

BACKGROUND

Transfer mechanisms between mother and unborn child are consisting of complex processes. For obvious reasons approval of pharmaceuticals is generally only possible for non-pregnant women. Before drugs are approved for pregnant women, they have to be studied in separate clinical trials. Any form of pre-clinical evidence concerning putative transport mechanisms through the placenta is an important decision-making support for regulatory authorization, especially in case of evidence that no transfer to the fetal circuit will occur and the role of the placenta in a possible transfer process has been clearly outlined.

Dual perfusion of a single placental lobule ex vivo is the only experimental model to study human placental transfer of substances in organized tissue. In comparison to other experimental methods results from perfusion experiments may predict more reliably fetal exposure to specific substances.

TECHNOLOGY

Separate artificial circuits for maternal and fetal compartments are set-up by cannulation of a placenta, incubated under physiological conditions. This setting (see scheme) allows observation of the exchange of substances between the maternal and the fetal circuit. The separate circuits are continuously monitored by a data logger and several parameters are collected to monitor viability and integrity both during and after perfusion by a computerized gas analyzer. These parameters include the values of pH, pO₂, pCO₂, lactate, glucose and perfusion pressure. At any time samples can be taken from both circuits in order to perform further analyses.

CHARACTERISTICS

- Model system for the transfer of substances to fetal circuit in late pregnancy.
- Imitation of in vivo situation of late pregnancy over several hours.
- Dual system with completely separated circuits.
- Open or closed circuits allow recirculation of medium.
- Physiological conditions: constant body temperature and oxygen concentration of 5-8%.
- Only human organ available for perfusion experiments at healthy conditions.

FIELDS OF APPLICATION

Test of pharmaceuticals relevant in pregnancy (e.g. biologics, antidepressants), nanoparticles, environmental pollutants and other substances with possible transfer to the fetal circuit or damages of the placenta.

ADVANTAGES

- Most closely resembles the in vivo situation.
- Can measure transfer over time and sampling is available from all compartments.
- Potential for avoiding animal experiments for toxicity testings.
- Testing in human organ leads to higher relevance of results.
- Standardized experimental conditions.
- Reprocessing of perfused tissue.
- Primary placental cells as complementary method available.
- Easy access to placenta material due to upright approval of ethics committee.
- Analysis software allows GLP-compliant documentation.

CONTACT

Dr. Heidi Schmitt
Technology Transfer Office
Auenbruggerplatz 2
A-8036 Graz
+43-316-385-72018
heidi.schmitt@medunigraz.at